UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,795	08/19/2003	Frederic J. DeSauvage	P5026R1	6007

25213 7590 02/19/2008

HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
YAO, LEI	
ART UNIT	**PAPER NUMBER**
1642	
MAIL DATE	**DELIVERY MODE**
02/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/643,795	DESAUVAGE ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-18* is/are pending in the application.

4a) Of the above claim(s) *18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Amendment and Arguments

The Amendment filed on 12/6/2007 in response to the previous Non-Final Office Action (9/20/2007) is acknowledged and has been entered.

Claims 16-18 are pending.

Claim 18 has been withdrawn for non-elected invention.

Claims 16-17, as drawn to a mehtod of diagnosing the prostate tumor comprising determining the levels of expressiing a gene encoding the peptide of SEQ ID NO: 123 by hybridization or PCR, are under consideration.

Rejection Maintained and Response to the Arguments

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 16 and 17 remain rejected under 35 U.S.C. 102(a) as being anticipated by Gish et al., (WO02/30268, published 4/18/2002, provided in the Office Action dated 10/11/2006) stated as the following:

Gish et al., disclose a method of diagnosing a prostate cancer by detecting a prostate cancer-associated transcript (mRNA) in a cell from a patient comprising determining a nucleic acid encoding a polypeptide, which is 99.6% identical to the amino acid sequence of SEQ ID NO: 123, different at first 4 amino acids (see sequence search; page 322-323 and 139, protein sequence, SEQ ID NO: 53 having

accession no: AA431407 or unigene ID No, Hs.98802, provided in previous office action). Gish et al., disclose the method comprising contacting a biological sample from a prostate patient with a polynucleotide probe that selectively hybridizes to the sequence (page 3). Gish et al., further disclose that the nucleic acid comprising mRNA expressed in prostate cancer sample is detected by *in situ* hybridization or PCR (page 59, 61, and 91-97, example 1). Gish et al., also disclose that expressing the specific prostate cancer gene in the prostate tumor tissue is 33.6 times higher (RI=33.6) compared to the normal prostate tissue (Table 4, page 139, line 3).

Since claimed method is not drawn to a specific oligonucleotide as primers or a probe for the in situ hybridization or RT-PCR, the method disclosed by Gish et al., anticipates the claimed method of diagnosing the presence of a prostate tumor comprising determining the higher levels of expression of a gene encoding the polypeptide shown as SEQ IDNO: 123 by an in situ hybridization or RT-PCR.

It is noted that the sequence search results are attached here and also available in SCOR if applicant needs more references related in this Office action.

Previous response to applicant's argument dated 7/20/2007 is also maintained for the reason of record as set forth in the Office action dated 9/20/2007.

The response has been carefully considered but is deemed not to be persuasive. Applicant argues that the DNA cited in the rejection does not encode the protein of SEQ ID NO: 123 and states:

> The Examiner relies on the nucleotide sequence shown as Gish's SEQ ID NO: 53 to conclude that the reference anticipates Applicants' currently pending claims.
> This sequence is not a gene encoding the polypeptide shown as SEQ ID NO: 123 as currently recited in claim 16. Although the Examiner cites a "sequence search, exhibit B" that accompanied the October 11, 2006 Office Action, this exhibit does not support the Examiner's position. The query sequence of the Examiner's search appears to be an amino acid sequence corresponding to residues 5-1170 of Applicants SEQ ID NO: 123 but the alleged database search result appears to correspond to a nucleotides 3-3371 of Gish's nucleic acid sequence shown as SEQ ID NO: 105. As such, the Examiner's exhibit B is unrelated to Gish's SEQ ID NO: 53 and therefore irrelevant to the asserted 102(a) rejection.

In response, the Office here would like to further clarify the Office's position related to search result and applicant's concerns as the following: The Office cited the WO document by Gish et al based on the sequence search result of SEQ ID NO: 123 against the coding DNA in the database RNG (N_Geneseq_8: year 1980-2006, attached here again and also see SCORE). The search result of sequence #53 (SEQ ID NO: 53, WO 02/30268) identifies a DNA having 3810 base pair (bp), in which the nucleotides at position 3-3371 encode a protein that is 100% identical to the amino acid sequence of SEQ ID NO: 123 recited in the claims except the N-terminal 4 amino acids. The text of the search result also indicates that the sequence #53 is listed on page 339-340 of the WO document, where, however, the

DNA of SEQ ID NO: 105 (not sequence #53) was described and listed (as stated in applicant's argument above). The more sequence search of database rnpm teaches that the DNA of SEQ ID NO: 105 is identical sequence to the DNA of sequence #53 from the database RNG, and both encode the instant claimed SEQ ID NO: 123 except the N-terminal 4 amino acids (see attached search result). Thus, based on the search results, the DNA of SEQ ID NO: 105 is a duplicate of the DNA of sequence #53 in the WO document. The sequence search result also indicates that the DNA of SEQ ID NO: 105 encodes a protein of SEQ ID NO: 106. The protein of SEQ ID NO: 106 is 1061 amino acid protein with 100% amino acid sequence identity to the claimed protein, SEQ ID NO: 123 at position 112-1127 and the first ATG as the start codon at position 324 of SEQ ID NO: 105 is used for translation and form the protein (SEQ ID NO: 106) with a deletion of 111 amino acids of at N-terminus of SEQ ID NO: 123. One skilled in the art would understand that the protein of SEQ ID NO: 106 is predicated based on the first appeared start codon ATG located at position 324 of the DNA (SEQ ID NO: 105) and would understand a long protein might be formed or predicted if there is another start codon before position 324 of the DNA of SEQ ID NO: 105. Since the claimed invention is drawn to a method comprising the step of determining the levels of expression of the gene encoding the protein of SEQ ID NO: 123 by in situ hybridization and RT-PCR analysis, the Office considers that the method of detecting the gene expression of sequence #53 or SEQ ID NO: 105 (12 nucleotides shorter than the DNA encoding a protein of SEQ ID NO: 123) would anticipate the claimed method step as stated in the rejection. Thus, the Office did not additionally provide the encoded protein sequence of SEQ ID NO: 106 as well as the protein alignment for applicant at the time of sending the Office action dated 9/27/2007. In response to the applicant's argument and concern, the sequence search results and alignment including the DNAs and proteins of SEQ ID NO: 105, 106 and #53 are enclosed in this Office Action (see attachments).

Again, as stated in the rejection, since claimed method does not recite a specific oligonucleotide as primers or a probe for the in situ hybridization or RT-PCR, the method step disclosed by Gish et al., would read on the claimed method of diagnosing the presence of a prostate tumor comprising determining expression of a gene encoding the polypeptide of SEQ IDNO: 123 by in situ hybridization or RT-PCR because one skilled in the art clearly know that the primer pair or a probe for hybridization

located anywhere in the coding region of the DNA (SEQ ID NO: 105) for the protein of SEQ ID NO: 106 would pick up the expressed gene product (such as RNA) that encodes a fragment of SEQ ID NO: 123, such as a protein of SEQ ID NO: 106, as well as the nucleotides encoding the entirety of the instant claimed protein of SEQ ID NO: 123 by the hybridization of in situ of RT-PCR. As such, again the method of Gish et al., teach each and every limitation of the claimed method, therefore, anticipate claimed invention. Thus, Applicant's argument has not been found persuasive, and the rejection is maintained for the reason of record.

2. Claims 16 and 17 remain rejected under 35 U.S.C. 102(e) as being anticipated by Gish et al., (US PG Pub. 2007/0014801, effective filing date, Jan 2001) as evidenced by sequence search result in database rnpm stated as the following:

> Gish et al., disclose a method of diagnosing a prostate cancer by detecting a prostate cancer-associated transcript (mRNA) in a cell from a patient comprising determining a nucleic acid encoding a polypeptide, which is 100% identical to the amino acid sequence of SEQ ID NO: 123 from amino acids 5-1127 (different at first 4 amino acids, see sequence search; SEQ ID NO: 105 having accession no: AI460004). Gish et al., disclose a method of detecting a prostate cancer-associated transcript in a cell from a patient, the method comprising contacting a biological sample from the patient with a polynucleotide that selectively hybridizes to a sequence (paragraph 0008). Gish et al., further disclose that the nucleic acid comprising mRNA expressed in prostate cancer sample is detected by *in situ* hybridization or PCR (paragraph 0093 and 0210). Gish et al., also disclose that expressing the specific prostate cancer gene (SEQ ID NO: 105, PEU5, having accession no: AI460004) in the prostate tumor tissue is up-regulated eight times compared to the normal prostate tissue (Table 3, page 127, line 3).
>
> Since claimed method is not drawn to a specific oligonucleotide as primers or a probe for in situ hybridization or RT-PCR, the method disclosed by Gish et al., anticipates the claimed method of diagnosing the presence of a prostate tumor comprising determining the higher levels of expression of a gene encoding the polypeptide shown as SEQ IDNO: 123 by an in situ hybridization or RT-PCR.

Applicant first presents the same argument, which has been responded above. Applicant further argues:

> it does not matter how many amino acid residues of a Gish II polypeptide overlap with SEQ ID NO: 123 because the critical fact overlooked by the Examiner is that the reference fails to disclose a nucleotide sequence encoding a polypeptide having the exact 1127 residue amino acid sequence of SEQ ID NO: 123.

In response, applicant is reminded again that claimed invention is not drawn to a product, instead, drawn to a method of diagnosing prostate cancer by determining the expression of a gene by hybridization of the

nucleotides encoding a protein of SEQ ID NO: 123 with an oligonucleotide in situ or RT-PCR. The claimed method recites only A step of determining the higher expression of a DNA encoding the protein of SEQ ID NO: 123 compared to the levels in the control sample, no specific primer set which recognizes only the nucleotides encoding SEQ ID NO: 123, not the nucleotides of Gish et al., are included in the claimed method. Gish et al., disclose a method of detecting the prostate cancer by determining the higher levels of the nucleotides of SEQ ID NO: 105 that encoded the entirety of the protein of SEQ ID NO: 123 except N-terminal four amino acids. The relationship of the sequences and sequence alignment between the proteins of SEQ ID NO: 123 of applicant and the protein of SEQ ID NO: 106 of Gish et al., has been discussed above. As such, one skilled in the art would consider the protein (SEQ ID NO: 106) of Gish et al is fragment of SEQ ID NO: 123 or an alternative spliced gene product. Since the protein of 106 is shorter than the protein of SEQ ID NO: 123 and the coding nucleotides of SEQ ID NO: 105 is 100% identical to the nucleotides encoding the protein of SEQ ID NO: 123, the method of Gish et al used for determination the gene expression of SEQ ID NO: 105 would inherently pick up the expressed nucleotides encoding the protein of SEQ ID NO: 123.

Applicant again argues:

> the Examiner erroneously states that SEQ ID NO: 105 is "different at [the] first 4 amino acids" when compared to Applicants' SEQ ID NO: 123. The translated 1016 residue amino acid sequence of the PEU5 gene (SEQ ID NO: 105) is shown on page 340 of Gish II as SEQ ID NO:106. The overlap between SEQ ID NO:106 and Applicants' SEQ ID NO:123 runs from the methionine residue at position 112 to the threonine residue at position 1127. As such, Gish II's SEQ ID NO:106 does not contain all the amino acids shown in SEQ ID NO:123, beginning at the methionine residue at position 1 and ending at the glutamine residue at position 111. Therefore, the difference between SEQ ID NO: 105 of Gish II and Applicants' SEQ ID NO: 123 is 111 amino acids and not the 4 amino acids argued by the Examiner.

and again:

> the translated polypeptide sequence of SEQ ID NO: 105 is the 1016 amino acid sequence shown as SEQ ID NO: 106. Despite the fact that Gish II provides the PEU5 polypeptide sequence, the Examiner has inexplicably concluded that the polypeptide includes an additional 111 amino acid residues (methionine 1 to glutamine 111 as discussed above) corresponding to the nucleotides 3-323 of SEQ ID NO: 105. However, Gish quite clearly discloses on page 339 of the sequence listing as originally filed that the coding sequence for SEQ ID NO:105 is "324-3374 (underlined sequences correspond to start and stop codons)". In the nucleotide sequence shown as SEQ ID NO: 105, an ATG methionine start codon is underlined at nucleotides 324-326 and a TAG stop codon is underlined at nucleotides 3372-3374.

In response, the Office agrees with applicant in part, which the protein of SEQ ID NO: 123 containing additional 111 amino acids at N-terminus is longer than the protein of SEQ ID NO: 106, however disagrees with applicant's statement that the protein encoded by SEQ ID NO: 105 is more different than the first 4 amino acids of applicant' SEQ ID NO: 123. The relationship of the sequences and alignment between the proteins of SEQ ID NO: 123 and the protein of SEQ ID NO: 106 has been discussed above. Moreover, the SEQ ID NO: 105 is 3810 nucleotide sequences that contains all the codons for the protein of SEQ ID NO: 123 except the first 12 nucleotides for the first 4 amino acids including the ATG start codon. Although Gish et al., predict a protein of SEQ ID NO:106 translated from the first codon ATG at position 324 of SEQ ID NO: 105 one skilled in the art would understand and conclude the protein of SEQ ID NO: 106 and protein of SEQ ID NO: 123 are encoded by the same gene. Thus, if the oligonucleotide primer designed within the coding region of both proteins except the primer including the first 12 nucleotides encoding the first 4 amino acids of SEQ ID NO: 123, the gene products of mRNA encoding the protein of SEQ ID NO: 123 or the protein of SEQ ID NO:106 would be hybridized by RT-PCR or in situ and the levels of gene expression encoding either of the proteins would be determined by such hybridization.

Again, as stated above, claimed invention is drawn a method of determining the gene expression by nucleotide hybridization. The method of Gish et al used for determination the gene expression of a nucleotides of SEQ ID NO: 105 would inherently pick up the expressed gene product encoding a protein of SEQ ID NO: 123 since the nucleotides of SEQ ID NO: 105 is 100% identical to the nucleotides encoding the protein of SEQ ID NO: 123 with missing just first 12 nucleotides of entirety of over 3800 nucleotides. Thus, applicant's argument has not been found persuasive, and the rejection is maintained for the reason of record.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao,
Examiner
Art Unit 1642

LY

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643